Clinical trial results:
A Randomized, Open-Label, Multicenter Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Co-Administration of ABT-493 and ABT-530 With and Without RBV in Subjects With Chronic Hepatitis C Virus (HCV) Genotypes 2, 3, 4, 5 or 6 Infection (SURVEYOR-II)

Summary

EudraCT number	2014-002927-90
Trial protocol	GB
Global end of trial date	23 February 2017

Results information

Result version number	v1 (current)
This version publication date	19 January 2018
First version publication date	19 January 2018

Trial information

Trial identification

Sponsor protocol code	M14-868

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02243293
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 001 800-633-9110,
Scientific contact	Stanley Wang, AbbVie, stanley.wang@abbvie.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this phase 2/3, open-label, multipart, multicenter study was to evaluate the efficacy, and safety of coadministration of ABT-493 and ABT-530 with and without ribavirin (RBV) in chronic HCV genotype 2 (GT2-), genotype 3 (GT3-), genotype 4 (GT4), genotype 5 (GT5-), or genotype 6 (GT6-) infected participants with or without cirrhosis.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 September 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 65
Country: Number of subjects enrolled	Canada: 54
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	New Zealand: 62
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 493
Worldwide total number of subjects	694
EEA total number of subjects	12

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	618
From 65 to 84 years	76
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrollment into arms H, I, K, M and N was not opened by AbbVie.

Pre-assignment

Screening details:

Intent-to-treat population: all participants who received at least 1 dose of study drug.

Period 1

Period 1 title	Overall Study (As Treated) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV genotype 2 (GT2) -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Arm title	Arm B

Arm description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir

Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Arm title	Arm C

Arm description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and weight-based ribavirin (RBV) divided twice daily (BID) for 12 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Investigational medicinal product name	ribavirin (RBV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Weight-based ribavirin (RBV) divided twice daily (BID).

Arm title	Arm D

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV genotype 3 (GT3) -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Arm title	Arm E

Arm description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Arm title	Arm F

Arm description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and weight-based ribavirin (RBV) divided BID for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Investigational medicinal product name	ribavirin (RBV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Weight-based ribavirin (RBV) divided twice daily (BID).

Arm title	Arm G

Arm description:

ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (40 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental

Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (40 mg) once daily (QD)

Arm title	Arm J

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 8 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Arm title	Arm L

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 8 weeks in HCV GT3 -infected treatment naïve and for 12 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Arm title	Arm O

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve participants with compensated cirrhosis and for 16 weeks in HCV GT3 -infected treatment-experienced participants with compensated cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Arm title	Arm P

Arm description:

ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and RBV (800 mg) QD for 12 weeks in HCV GT3-infected treatment naïve and treatment-experienced participants with compensated cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493
Investigational medicinal product code	
Other name	glecaprevir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg once daily (QD)

Investigational medicinal product name	ABT-530
Investigational medicinal product code	
Other name	pibrentasvir
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-530 (120 mg) once daily (QD)

Investigational medicinal product name	ribavirin (RBV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ribavirin (RBV) 800 mg once daily (QD).

Arm title	Arm Q1

Arm description:

ABT-493/ ABT-530 (300 mg/ 120mg) once daily (QD) for 12 weeks in HCV GT3 -infected treatment naïve participants with cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493/ABT-530
Investigational medicinal product code	
Other name	ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-493 (300 mg) co-formulated ABT-530 (120 mg) once daily (QD)

Arm title	Arm Q2

Arm description:

ABT-493/ ABT-530 (300 mg/ 120mg) once daily (QD) for 12 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493/ABT-530
Investigational medicinal product code	
Other name	ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-493 (300 mg) co-formulated ABT-530 (120 mg) once daily (QD)

Arm title	Arm R1

Arm description:

ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 16 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493/ABT-530
Investigational medicinal product code	
Other name	ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-493 (300 mg) co-formulated ABT-530 (120 mg) once daily (QD)

Arm title	Arm R2

Arm description:

ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 16 weeks in HCV GT3 -infected treatment experienced participants with cirrhosis.

Arm type	Experimental
Investigational medicinal product name	ABT-493/ABT-530
Investigational medicinal product code	
Other name	ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

ABT-493 (300 mg) co-formulated ABT-530 (120 mg) once daily (QD)

Arm title	Arm S1

Arm description:	
ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 8 weeks in HCV GT2 infected treatment naïve and treatment experienced participants without cirrhosis.	
Arm type	Experimental
Investigational medicinal product name	ABT-493/ABT-530
Investigational medicinal product code	
Other name	ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
ABT-493 (300 mg) co-formulated ABT-530 (120 mg) once daily (QD)	
Arm title	Arm S2
Arm description:	
ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 8 weeks in HCV GT4-6 infected treatment naïve and treatment experienced participants without cirrhosis.	
Arm type	Experimental
Investigational medicinal product name	ABT-493/ABT-530
Investigational medicinal product code	
Other name	ABT-493 also known as glecaprevir, ABT-530 also known as pibrentasvir, MAVIRET
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
ABT-493 (300 mg) co-formulated ABT-530 (120 mg) once daily (QD)	

Number of subjects in period 1[1]	Arm A	Arm B	Arm C
Started	25	24	25
Completed	23	23	24
Not completed	2	1	1
Consent withdrawn by subject	1	-	-
Enrolled into a Re-treatment Study	-	-	-
Adverse event	1	-	-
Lost to follow-up	-	1	1

Number of subjects in period 1[1]	Arm D	Arm E	Arm F
Started	30	30	31
Completed	29	30	31
Not completed	1	0	0
Consent withdrawn by subject	-	-	-
Enrolled into a Re-treatment Study	-	-	-
Adverse event	-	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1[1]	Arm G	Arm J	Arm L
Started	30	54	53
Completed	27	53	50
Not completed	3	1	3
Consent withdrawn by subject	-	1	1
Enrolled into a Re-treatment Study	-	-	-
Adverse event	-	-	-
Lost to follow-up	3	-	2

Number of subjects in period 1[1]	Arm O	Arm P	Arm Q1
Started	28	27	40
Completed	27	26	37
Not completed	1	1	3
Consent withdrawn by subject	-	-	-
Enrolled into a Re-treatment Study	1	-	-
Adverse event	-	1	-
Lost to follow-up	-	-	3

Number of subjects in period 1[1]	Arm Q2	Arm R1	Arm R2
Started	22	22	47
Completed	21	22	47
Not completed	1	0	0
Consent withdrawn by subject	-	-	-
Enrolled into a Re-treatment Study	-	-	-
Adverse event	-	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1[1]	Arm S1	Arm S2
Started	145	58
Completed	143	55
Not completed	2	3
Consent withdrawn by subject	-	1
Enrolled into a Re-treatment Study	-	-
Adverse event	1	-
Lost to follow-up	1	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The subject disposition section refers only to the subjects who have received study drug. Three subjects (1 subject each in arms E, J and R2 respectively) were randomized but didn't receive study drug.

Baseline characteristics

Reporting groups

Reporting group title	Arm A
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV genotype 2 (GT2) -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm B
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm C
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and weight-based ribavirin (RBV) divided twice daily (BID) for 12 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm D
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV genotype 3 (GT3) -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm E
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm F
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and weight-based ribavirin (RBV) divided BID for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm G
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (40 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm J
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 8 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm L
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 8 weeks in HCV GT3 -infected treatment naïve and for 12 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.	
Reporting group title	Arm O
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve participants with compensated cirrhosis and for 16 weeks in HCV GT3 -infected treatment-experienced participants with compensated cirrhosis.	
Reporting group title	Arm P
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and RBV (800 mg) QD for 12 weeks in HCV GT3-infected treatment naïve and treatment-experienced participants with compensated cirrhosis.	
Reporting group title	Arm Q1
Reporting group description:	
ABT-493/ ABT-530 (300 mg/ 120mg) once daily (QD) for 12 weeks in HCV GT3 -infected treatment naïve participants with cirrhosis.	

Reporting group title	Arm Q2
Reporting group description:	
ABT-493/ ABT-530 (300 mg/ 120mg) once daily (QD) for 12 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.	
Reporting group title	Arm R1
Reporting group description:	
ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 16 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.	
Reporting group title	Arm R2
Reporting group description:	
ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 16 weeks in HCV GT3 -infected treatment experienced participants with cirrhosis.	
Reporting group title	Arm S1
Reporting group description:	
ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 8 weeks in HCV GT2 infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm S2
Reporting group description:	
ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 8 weeks in HCV GT4-6 infected treatment naïve and treatment experienced participants without cirrhosis.	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	25	24	25
Age categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
< 65 years	21	21	22
>= 65 years	4	3	3
Gender categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
Female	9	11	7
Male	16	13	18

Reporting group values	Arm D	Arm E	Arm F
Number of subjects	30	30	31
Age categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
< 65 years	28	29	30
>= 65 years	2	1	1
Gender categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
Female	11	16	12
Male	19	14	19

Reporting group values	Arm G	Arm J	Arm L
Number of subjects	30	54	53

Age categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
< 65 years	28	44	52
>= 65 years	2	10	1
Gender categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
Female	15	21	21
Male	15	33	32

Reporting group values	Arm O	Arm P	Arm Q1
Number of subjects	28	27	40
Age categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
< 65 years	26	24	38
>= 65 years	2	3	2
Gender categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
Female	13	9	16
Male	15	18	24

Reporting group values	Arm Q2	Arm R1	Arm R2
Number of subjects	22	22	47
Age categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
< 65 years	18	19	39
>= 65 years	4	3	8
Gender categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
Female	8	8	11
Male	14	14	36

Reporting group values	Arm S1	Arm S2	Total
Number of subjects	145	58	691
Age categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
< 65 years	128	49	616
>= 65 years	17	9	75
Gender categorical			
All participants who received atleast 1 dose of study drug (ITT population) are analyzed.			
Units: Subjects			
Female	84	21	293
Male	61	37	398

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV genotype 2 (GT2) -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm B
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm C
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and weight-based ribavirin (RBV) divided twice daily (BID) for 12 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm D
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV genotype 3 (GT3) -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm E
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm F
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and weight-based ribavirin (RBV) divided BID for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm G
Reporting group description:	
ABT-493 (200 mg) once daily (QD) co-administered with ABT-530 (40 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm J
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 8 weeks in HCV GT2 -infected treatment naïve and treatment experienced participants without cirrhosis.	
Reporting group title	Arm L
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 8 weeks in HCV GT3 -infected treatment naïve and for 12 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.	
Reporting group title	Arm O
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD for 12 weeks in HCV GT3 -infected treatment naïve participants with compensated cirrhosis and for 16 weeks in HCV GT3 -infected treatment-experienced participants with compensated cirrhosis.	
Reporting group title	Arm P
Reporting group description:	
ABT-493 (300 mg) once daily (QD) co-administered with ABT-530 (120 mg) QD and RBV (800 mg) QD for 12 weeks in HCV GT3-infected treatment naïve and treatment-experienced participants with compensated cirrhosis.	
Reporting group title	Arm Q1
Reporting group description:	
ABT-493/ ABT-530 (300 mg/ 120mg) once daily (QD) for 12 weeks in HCV GT3 -infected treatment naïve participants with cirrhosis.	

Reporting group title	Arm Q2

Reporting group description:

ABT-493/ ABT-530 (300 mg/ 120mg) once daily (QD) for 12 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.

Reporting group title	Arm R1

Reporting group description:

ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 16 weeks in HCV GT3 -infected treatment experienced participants without cirrhosis.

Reporting group title	Arm R2

Reporting group description:

ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 16 weeks in HCV GT3 -infected treatment experienced participants with cirrhosis.

Reporting group title	Arm S1

Reporting group description:

ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 8 weeks in HCV GT2 infected treatment naïve and treatment experienced participants without cirrhosis.

Reporting group title	Arm S2

Reporting group description:

ABT-493/ ABT-530 (300 mg/ 120 mg) QD for 8 weeks in HCV GT4-6 infected treatment naïve and treatment experienced participants without cirrhosis.

Primary: Percentage of Participants With Sustained Virologic Response 12 Weeks Post-treatment (SVR12)

End point title	Percentage of Participants With Sustained Virologic Response 12 Weeks Post-treatment (SVR12)[1]

End point description:

SVR12 was defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification [<LLOQ]) 12 weeks after the last dose of study drug.

End point type	Primary

End point timeframe:

12 weeks after the last actual dose of study drug

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive data are summarized for this end point per protocol.

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25[2]	24[3]	25[4]	30[5]
Units: percentage of participants				
number (confidence interval 95%)	96.0 (80.5 to 99.3)	100.0 (86.2 to 100.0)	100.0 (86.7 to 100.0)	93.3 (78.7 to 98.2)

Notes:

[2] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[3] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[4] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[5] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm E	Arm F	Arm G	Arm J

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30[6]	31[7]	30[8]	54[9]
Units: percentage of participants				
number (confidence interval 95%)	93.3 (78.7 to 98.2)	93.5 (79.3 to 98.2)	83.3 (66.4 to 92.7)	98.1 (90.2 to 99.7)

Notes:

[6] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[7] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[8] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[9] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm L	Arm O	Arm P	Arm Q1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[10]	28	27[11]	40[12]
Units: percentage of participants				
number (confidence interval 95%)	94.3 (84.6 to 98.1)	96.4 (82.3 to 99.4)	100.0 (87.5 to 100.0)	97.5 (87.1 to 99.6)

Notes:

[10] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[11] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[12] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm Q2	Arm R1	Arm R2	Arm S1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[13]	22[14]	47[15]	145[16]
Units: percentage of participants				
number (confidence interval 95%)	90.9 (72.2 to 97.5)	95.5 (78.2 to 99.2)	95.7 (85.8 to 98.8)	97.9 (94.1 to 99.3)

Notes:

[13] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[14] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[15] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[16] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm S2			
Subject group type	Reporting group			
Number of subjects analysed	58[17]			
Units: percentage of participants				
number (confidence interval 95%)	93.1 (83.6 to 97.3)			

Notes:

[17] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Genotype 2 (GT2) Direct-acting Antiviral Agents (DAA)-Naive Participants (in Part 4, Arm S1) With Sustained Virologic Response 12 Weeks Post-treatment (SVR12) as Compared to Historical Control

End point title	Percentage of Genotype 2 (GT2) Direct-acting Antiviral Agents (DAA)-Naive Participants (in Part 4, Arm S1) With Sustained Virologic Response 12 Weeks Post-treatment (SVR12) as Compared to Historical Control[18][19]

End point description:

SVR12 was defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification [<LLOQ]) 12 weeks after the last dose of study drug.

End point type	Primary

End point timeframe:

12 weeks after the last actual dose of study drug

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The percentage of subjects (95% CI, calculated using the normal approximation to the binomial distribution) achieving SVR12 was 98.5% (96.5 to 100.0). The non-inferiority of the rate of SVR12 as compared to historical control (in genotype 2 (GT2) DAA-naive participants in Part 4, arm S1) was analyzed; the lower confidence bound of the 2-sided 95% confidence interval (95% CI) for the percentage of participants with SVR12 must exceed 89% to achieve non-inferiority.
[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was analyzed only in subjects in genotype 2 (GT2) DAA-Naive Participants (in Part 4, Arm S1).

End point values	Arm S1			
Subject group type	Reporting group			
Number of subjects analysed	137[20]			
Units: percentage of participants				
number (confidence interval 95%)	98.5 (96.5 to 100.0)			

Notes:

[20] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response 4 Weeks Post-treatment (SVR4)

End point title	Percentage of Participants With Sustained Virologic Response 4 Weeks Post-treatment (SVR4)

End point description:

SVR4 was defined as plasma hepatitis C virus ribonucleic acid (HCV RNA) level less than the lower limit of quantification [<LLOQ]) 4 weeks after the last dose of study drug.

End point type	Secondary

End point timeframe:

4 weeks after the last actual dose of study drug

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25[21]	24[22]	25[23]	30[24]
Units: percentage of participants				
number (confidence interval 95%)	96.0 (80.5 to 99.3)	100.0 (86.2 to 100.0)	100.0 (86.7 to 100.0)	93.3 (78.7 to 98.2)

Notes:

[21] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[22] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[23] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[24] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm E	Arm F	Arm G	Arm J
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30[25]	31[26]	30[27]	54[28]
Units: percentage of participants				
number (confidence interval 95%)	93.3 (78.7 to 98.2)	93.5 (79.3 to 98.2)	93.3 (78.7 to 98.2)	98.1 (90.2 to 99.7)

Notes:

[25] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[26] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[27] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[28] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm L	Arm O	Arm P	Arm Q1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[29]	28[30]	27[31]	40[32]
Units: percentage of participants				
number (confidence interval 95%)	96.2 (87.2 to 99.0)	96.4 (82.3 to 99.4)	100.0 (87.5 to 100.0)	97.5 (87.1 to 99.6)

Notes:

[29] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[30] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[31] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[32] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm Q2	Arm R1	Arm R2	Arm S1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[33]	22[34]	47[35]	145[36]
Units: percentage of participants				
number (confidence interval 95%)	95.5 (78.2 to 99.2)	95.5 (78.2 to 99.2)	95.7 (85.8 to 98.8)	97.9 (94.1 to 99.3)

Notes:

[33] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

[34] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[35] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.
[36] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

End point values	Arm S2			
Subject group type	Reporting group			
Number of subjects analysed	58[37]			
Units: percentage of participants				
number (confidence interval 95%)	98.3 (90.9 to 99.7)			

Notes:

[37] - All participants who received at least 1 dose of study drug; missing data imputed as nonresponders.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With On-treatment Virologic Failure

End point title	Percentage of Participants With On-treatment Virologic Failure

End point description:

On-treatment virologic failure was defined as confirmed HCV RNA ≥ LLOQ after HCV RNA < LLOQ during treatment; confirmed increase of > 1 log(subscript)10(subscript) IU/mL above the lowest value post-baseline in HCV RNA during treatment; or HCV RNA ≥ LLOQ at end of treatment with at least 6 weeks of treatment.

End point type	Secondary

End point timeframe:

Up to end of treatment (treatment week 8, 12 or 16 depending on arm) or premature discontinuation from treatment

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25[38]	24[39]	25[40]	30[41]
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 13.3)	0 (0.0 to 13.8)	0 (0.0 to 13.3)	0 (0.0 to 11.4)

Notes:

[38] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

[39] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

[40] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

[41] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

End point values	Arm E	Arm F	Arm G	Arm J
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30[42]	31[43]	30[44]	54[45]
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 11.4)	3.2 (0.6 to 16.2)	3.3 (0.6 to 16.7)	0 (0.0 to 6.6)

Notes:
[42] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[43] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[44] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[45] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

End point values	Arm L	Arm O	Arm P	Arm Q1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53[46]	28[47]	27[48]	40[49]
Units: percentage of participants				
number (confidence interval 95%)	1.9 (0.3 to 9.9)	0 (0.0 to 12.1)	0 (0.0 to 12.5)	0 (0.0 to 8.8)

Notes:
[46] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[47] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[48] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[49] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

End point values	Arm Q2	Arm R1	Arm R2	Arm S1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[50]	22[51]	47[52]	145[53]
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 14.9)	0 (0.0 to 14.9)	2.1 (0.4 to 11.1)	0 (0.0 to 2.6)

Notes:
[50] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[51] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[52] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.
[53] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

End point values	Arm S2			
Subject group type	Reporting group			
Number of subjects analysed	58[54]			
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 6.2)			

Notes:
[54] - All participants who received at least 1 dose of study drug (ITT population) with evaluable data.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Post-treatment Relapse

End point title	Percentage of Participants With Post-treatment Relapse

End point description:

Post-treatment relapse was defined as confirmed HCV RNA ≥ LLOQ between the end of treatment and 12 weeks after the last dose of study drug among participants who completed treatment with HCV RNA levels < LLOQ at the end of treatment, excluding reinfection.

End point type	Secondary

End point timeframe:

From the end of treatment through 12 weeks after the last dose of study drug

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24[55]	24[56]	25[57]	29[58]
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 13.8)	0 (0.0 to 13.8)	0 (0.0 to 13.3)	3.4 (0.6 to 17.2)

Notes:

[55] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[56] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[57] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[58] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.

End point values	Arm E	Arm F	Arm G	Arm J
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30[59]	28[60]	28[61]	53[62]
Units: percentage of participants				
number (confidence interval 95%)	6.7 (1.8 to 21.3)	0 (0.0 to 12.1)	7.1 (2.0 to 22.6)	0 (0.0 to 6.8)

Notes:

[59] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[60] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[61] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[62] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.

End point values	Arm L	Arm O	Arm P	Arm Q1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51[63]	28[64]	27[65]	39[66]
Units: percentage of participants				
number (confidence interval 95%)	2.0 (0.3 to 10.3)	3.6 (0.6 to 17.7)	0 (0.0 to 12.5)	0 (0.0 to 9.0)

Notes:

[63] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[64] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[65] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[66] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.

End point values	Arm Q2	Arm R1	Arm R2	Arm S1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22[67]	22[68]	46[69]	144[70]
Units: percentage of participants				
number (confidence interval 95%)	9.1 (2.5 to 27.8)	4.5 (0.8 to 21.8)	2.2 (0.4 to 11.3)	1.4 (0.4 to 4.9)

Notes:

[67] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[68] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[69] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.
[70] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.

End point values	Arm S2			
Subject group type	Reporting group			
Number of subjects analysed	57[71]			
Units: percentage of participants				
number (confidence interval 95%)	0 (0.0 to 6.3)			

Notes:

[71] - ITT subjects with evaluable data, completed treatment, and had HCV RNA <LLOQ at the final treatment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from the time of study drug administration until 30 days after the last dose of study drug (up to 20 weeks).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any adverse event (AE) or serious adverse event (SAE) with an onset date that is after the first dose of study drug until 30 days after the last dose of study drug and were collected whether elicited or spontaneously reported by the participant.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm B
Reporting group description: -	
Reporting group title	Arm C
Reporting group description: -	
Reporting group title	Arm D
Reporting group description: -	
Reporting group title	Arm E
Reporting group description: -	
Reporting group title	Arm F
Reporting group description: -	
Reporting group title	Arm G
Reporting group description: -	
Reporting group title	Arm J
Reporting group description: -	
Reporting group title	Arm L
Reporting group description: -	
Reporting group title	Arm O
Reporting group description: -	
Reporting group title	Arm P
Reporting group description: -	
Reporting group title	Arm Q1
Reporting group description: -	
Reporting group title	Arm Q2
Reporting group description: -	
Reporting group title	Arm R1
Reporting group description: -	
Reporting group title	Arm R2
Reporting group description: -	
Reporting group title	Arm S1
Reporting group description: -	
Reporting group title	Arm S2

Reporting group description: -

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC NEOPLASM			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
TIBIA FRACTURE			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ANGINA PECTORIS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
UMBILICAL HERNIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DELUSIONAL DISORDER, UNSPECIFIED TYPE			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

APPENDICITIS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm D	Arm E	Arm F
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC NEOPLASM			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
TIBIA FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ANGINA PECTORIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
UMBILICAL HERNIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DELUSIONAL DISORDER, UNSPECIFIED TYPE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm G	Arm J	Arm L
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC NEOPLASM			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
TIBIA FRACTURE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ANGINA PECTORIS			

subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
UMBILICAL HERNIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DELUSIONAL DISORDER, UNSPECIFIED TYPE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			

subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm O	Arm P	Arm Q1
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 28 (7.14%)	2 / 27 (7.41%)	1 / 40 (2.50%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC NEOPLASM			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
TIBIA FRACTURE			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ANGINA PECTORIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
UMBILICAL HERNIA			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DELUSIONAL DISORDER, UNSPECIFIED TYPE			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm Q2	Arm R1	Arm R2
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	3 / 47 (6.38%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLON CANCER			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC NEOPLASM			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
TIBIA FRACTURE			

subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ANGINA PECTORIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
UMBILICAL HERNIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
DELUSIONAL DISORDER, UNSPECIFIED TYPE			

subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCHIZOPHRENIA			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Arm S1	Arm S2	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 145 (1.38%)	1 / 58 (1.72%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-CELL LYMPHOMA			

subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLON CANCER			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC NEOPLASM			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
TIBIA FRACTURE			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ANGINA PECTORIS			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
UMBILICAL HERNIA			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
DELUSIONAL DISORDER, UNSPECIFIED TYPE			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCHIZOPHRENIA			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
APPENDICITIS			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			

subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 25 (48.00%)	11 / 24 (45.83%)	22 / 25 (88.00%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	3 / 25 (12.00%)
occurrences (all)	0	1	3
General disorders and administration site conditions			
ENERGY INCREASED			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	2 / 25 (8.00%)	3 / 24 (12.50%)	10 / 25 (40.00%)
occurrences (all)	3	3	10
FEELING HOT			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal			

disorders			
COUGH			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
DYSPNOEA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	3
NASAL CONGESTION			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
RHINORRHOEA			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	2 / 25 (8.00%)
occurrences (all)	0	1	2
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
DEPRESSION			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
EMOTIONAL DISORDER			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
IRRITABILITY			

subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
MOOD SWINGS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
BLOOD BILIRUBIN UNCONJUGATED INCREASED			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
HAEMATOCRIT DECREASED			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	4 / 25 (16.00%)
occurrences (all)	0	0	5
WEIGHT DECREASED			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	2 / 25 (8.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
DYSGEUSIA			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
HEADACHE			
subjects affected / exposed	1 / 25 (4.00%)	3 / 24 (12.50%)	6 / 25 (24.00%)
occurrences (all)	1	3	6
HYPOAESTHESIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
MIGRAINE			

subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	0 / 25 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL PAIN			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
CONSTIPATION			
subjects affected / exposed	1 / 25 (4.00%)	1 / 24 (4.17%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
DIARRHOEA			
subjects affected / exposed	4 / 25 (16.00%)	1 / 24 (4.17%)	6 / 25 (24.00%)
occurrences (all)	4	1	7
DYSPEPSIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	3
GASTROOESOPHAGEAL REFLUX DISEASE			

subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
NAUSEA			
subjects affected / exposed	3 / 25 (12.00%)	1 / 24 (4.17%)	8 / 25 (32.00%)
occurrences (all)	3	1	9
TOOTHACHE			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	3 / 25 (12.00%)
occurrences (all)	0	1	4
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
PRURITUS			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
RASH			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	3
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
BACK PAIN			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
MUSCULOSKELETAL PAIN			

subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 25 (0.00%)	1 / 24 (4.17%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
NECK PAIN			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	2 / 25 (8.00%)	0 / 24 (0.00%)	1 / 25 (4.00%)
occurrences (all)	2	0	1
GASTROENTERITIS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	2 / 25 (8.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	4 / 25 (16.00%)
occurrences (all)	1	0	4
TOOTH ABSCESS			
subjects affected / exposed	0 / 25 (0.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	1 / 25 (4.00%)	1 / 24 (4.17%)	5 / 25 (20.00%)
occurrences (all)	1	1	5
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 25 (0.00%)	2 / 24 (8.33%)	0 / 25 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 25 (4.00%)	0 / 24 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Arm D	Arm E	Arm F
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 30 (63.33%)	20 / 30 (66.67%)	23 / 31 (74.19%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ENERGY INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
FATIGUE			
subjects affected / exposed	6 / 30 (20.00%)	5 / 30 (16.67%)	12 / 31 (38.71%)
occurrences (all)	6	5	13
FEELING HOT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
PYREXIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	4 / 31 (12.90%)
occurrences (all)	1	2	5
DYSPNOEA			

subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	3 / 31 (9.68%)
occurrences (all)	2	0	3
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
NASAL CONGESTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
DEPRESSION			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	3	0
EMOTIONAL DISORDER			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	3 / 31 (9.68%)
occurrences (all)	1	2	3
IRRITABILITY			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	4
MOOD SWINGS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
BLOOD BILIRUBIN UNCONJUGATED INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
HAEMATOCRIT DECREASED			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	4 / 31 (12.90%)
occurrences (all)	0	0	5
WEIGHT DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	5 / 31 (16.13%)
occurrences (all)	1	1	5
DYSGEUSIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
HEADACHE			
subjects affected / exposed	4 / 30 (13.33%)	3 / 30 (10.00%)	6 / 31 (19.35%)
occurrences (all)	4	3	8
HYPOAESTHESIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
MIGRAINE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2

Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
CONSTIPATION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	3
DIARRHOEA			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	2 / 31 (6.45%)
occurrences (all)	3	1	3
DYSPEPSIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	3
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
NAUSEA			
subjects affected / exposed	2 / 30 (6.67%)	6 / 30 (20.00%)	11 / 31 (35.48%)
occurrences (all)	2	6	11
TOOTHACHE			

subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	4 / 31 (12.90%)
occurrences (all)	0	1	4
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
RASH			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
BACK PAIN			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	1	1	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
NECK PAIN			

subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	2	1
GASTROENTERITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
PHARYNGITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
SINUSITIS			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	1	3	1
TOOTH ABSCESS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 30 (13.33%)	1 / 30 (3.33%)	1 / 31 (3.23%)
occurrences (all)	4	1	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1

Non-serious adverse events	Arm G	Arm J	Arm L
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 30 (60.00%)	26 / 54 (48.15%)	40 / 53 (75.47%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	2 / 53 (3.77%)
occurrences (all)	0	1	2
General disorders and administration site conditions			
ENERGY INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	2 / 54 (3.70%)	0 / 53 (0.00%)
occurrences (all)	0	2	0
FATIGUE			
subjects affected / exposed	2 / 30 (6.67%)	7 / 54 (12.96%)	15 / 53 (28.30%)
occurrences (all)	3	7	15
FEELING HOT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	2 / 30 (6.67%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	2 / 53 (3.77%)
occurrences (all)	0	1	2
DYSPNOEA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 30 (3.33%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
NASAL CONGESTION			

subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 54 (0.00%)	4 / 53 (7.55%)
occurrences (all)	1	0	4
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
RHINORRHOEA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	1 / 30 (3.33%)	4 / 54 (7.41%)	1 / 53 (1.89%)
occurrences (all)	1	4	1
DEPRESSION			
subjects affected / exposed	2 / 30 (6.67%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	2	0	0
EMOTIONAL DISORDER			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	1 / 30 (3.33%)	3 / 54 (5.56%)	5 / 53 (9.43%)
occurrences (all)	1	3	5
IRRITABILITY			
subjects affected / exposed	0 / 30 (0.00%)	2 / 54 (3.70%)	0 / 53 (0.00%)
occurrences (all)	0	2	0
MOOD SWINGS			
subjects affected / exposed	1 / 30 (3.33%)	0 / 54 (0.00%)	3 / 53 (5.66%)
occurrences (all)	1	0	3
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN UNCONJUGATED INCREASED			

subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
HAEMATOCRIT DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
DYSGEUSIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
HEADACHE			
subjects affected / exposed	5 / 30 (16.67%)	6 / 54 (11.11%)	17 / 53 (32.08%)
occurrences (all)	5	7	20
HYPOAESTHESIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
MIGRAINE			
subjects affected / exposed	0 / 30 (0.00%)	2 / 54 (3.70%)	0 / 53 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	4 / 53 (7.55%)
occurrences (all)	0	0	5
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 30 (0.00%)	2 / 54 (3.70%)	3 / 53 (5.66%)
occurrences (all)	0	2	3
ABDOMINAL PAIN			
subjects affected / exposed	0 / 30 (0.00%)	2 / 54 (3.70%)	3 / 53 (5.66%)
occurrences (all)	0	2	4
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
CONSTIPATION			
subjects affected / exposed	1 / 30 (3.33%)	3 / 54 (5.56%)	3 / 53 (5.66%)
occurrences (all)	1	3	3
DIARRHOEA			
subjects affected / exposed	2 / 30 (6.67%)	4 / 54 (7.41%)	8 / 53 (15.09%)
occurrences (all)	2	4	9
DYSPEPSIA			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	2 / 53 (3.77%)
occurrences (all)	0	0	2
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	1 / 53 (1.89%)
occurrences (all)	0	1	1
NAUSEA			
subjects affected / exposed	0 / 30 (0.00%)	5 / 54 (9.26%)	4 / 53 (7.55%)
occurrences (all)	0	6	5
TOOTHACHE			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	4 / 53 (7.55%)
occurrences (all)	0	0	4
VOMITING			

subjects affected / exposed	2 / 30 (6.67%)	3 / 54 (5.56%)	2 / 53 (3.77%)
occurrences (all)	2	3	3
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	1 / 30 (3.33%)	1 / 54 (1.85%)	4 / 53 (7.55%)
occurrences (all)	1	1	5
RASH			
subjects affected / exposed	1 / 30 (3.33%)	0 / 54 (0.00%)	3 / 53 (5.66%)
occurrences (all)	1	0	3
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 30 (6.67%)	2 / 54 (3.70%)	2 / 53 (3.77%)
occurrences (all)	2	2	2
BACK PAIN			
subjects affected / exposed	2 / 30 (6.67%)	3 / 54 (5.56%)	1 / 53 (1.89%)
occurrences (all)	2	3	1
MUSCLE SPASMS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 30 (3.33%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	1
MYALGIA			
subjects affected / exposed	1 / 30 (3.33%)	0 / 54 (0.00%)	4 / 53 (7.55%)
occurrences (all)	1	0	4
NECK PAIN			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Infections and infestations			

BRONCHITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 30 (0.00%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	2 / 30 (6.67%)	1 / 54 (1.85%)	3 / 53 (5.66%)
occurrences (all)	2	1	3
PHARYNGITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 30 (0.00%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
TOOTH ABSCESS			
subjects affected / exposed	2 / 30 (6.67%)	0 / 54 (0.00%)	1 / 53 (1.89%)
occurrences (all)	2	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 30 (3.33%)	1 / 54 (1.85%)	4 / 53 (7.55%)
occurrences (all)	1	1	5
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 30 (3.33%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 30 (3.33%)	1 / 54 (1.85%)	0 / 53 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	Arm O	Arm P	Arm Q1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 28 (71.43%)	21 / 27 (77.78%)	30 / 40 (75.00%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ENERGY INCREASED			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	3 / 28 (10.71%)	8 / 27 (29.63%)	5 / 40 (12.50%)
occurrences (all)	3	8	6
FEELING HOT			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 28 (0.00%)	3 / 27 (11.11%)	1 / 40 (2.50%)
occurrences (all)	0	3	1
DYSPNOEA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0

RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
DEPRESSION			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
EMOTIONAL DISORDER			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
INSOMNIA			
subjects affected / exposed	0 / 28 (0.00%)	5 / 27 (18.52%)	1 / 40 (2.50%)
occurrences (all)	0	5	1
IRRITABILITY			
subjects affected / exposed	0 / 28 (0.00%)	4 / 27 (14.81%)	1 / 40 (2.50%)
occurrences (all)	0	4	1
MOOD SWINGS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
BLOOD BILIRUBIN UNCONJUGATED INCREASED			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
HAEMATOCRIT DECREASED			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
HAEMOGLOBIN DECREASED			

subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	2 / 28 (7.14%)	4 / 27 (14.81%)	4 / 40 (10.00%)
occurrences (all)	2	4	4
DYSGEUSIA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
HEADACHE			
subjects affected / exposed	5 / 28 (17.86%)	9 / 27 (33.33%)	10 / 40 (25.00%)
occurrences (all)	5	11	11
HYPOAESTHESIA			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
MIGRAINE			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
ABDOMINAL DISTENSION			
subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
ABDOMINAL PAIN			

subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	2 / 40 (5.00%)
occurrences (all)	0	2	2
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
CONSTIPATION			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
DIARRHOEA			
subjects affected / exposed	6 / 28 (21.43%)	1 / 27 (3.70%)	4 / 40 (10.00%)
occurrences (all)	6	1	4
DYSPEPSIA			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
NAUSEA			
subjects affected / exposed	3 / 28 (10.71%)	7 / 27 (25.93%)	4 / 40 (10.00%)
occurrences (all)	3	7	4
TOOTHACHE			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	1 / 40 (2.50%)
occurrences (all)	0	1	1
VOMITING			
subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	2 / 40 (5.00%)
occurrences (all)	2	1	2
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
PRURITUS			

subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	1 / 40 (2.50%)
occurrences (all)	1	2	1
RASH			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	1 / 40 (2.50%)
occurrences (all)	2	0	1
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	1 / 40 (2.50%)
occurrences (all)	0	2	1
BACK PAIN			
subjects affected / exposed	0 / 28 (0.00%)	3 / 27 (11.11%)	4 / 40 (10.00%)
occurrences (all)	0	3	4
MUSCLE SPASMS			
subjects affected / exposed	0 / 28 (0.00%)	3 / 27 (11.11%)	1 / 40 (2.50%)
occurrences (all)	0	3	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	1 / 40 (2.50%)
occurrences (all)	2	0	1
MYALGIA			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
GASTROENTERITIS			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	0 / 40 (0.00%)
occurrences (all)	1	2	0
GASTROENTERITIS VIRAL			

subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	3 / 40 (7.50%)
occurrences (all)	0	1	3
NASOPHARYNGITIS			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	2 / 40 (5.00%)
occurrences (all)	0	1	2
PHARYNGITIS			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
SINUSITIS			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
TOOTH ABSCESS			
subjects affected / exposed	0 / 28 (0.00%)	0 / 27 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 28 (17.86%)	2 / 27 (7.41%)	3 / 40 (7.50%)
occurrences (all)	5	2	3
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	2 / 40 (5.00%)
occurrences (all)	1	1	2
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	1 / 40 (2.50%)
occurrences (all)	2	0	1

Non-serious adverse events	Arm Q2	Arm R1	Arm R2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 22 (54.55%)	13 / 22 (59.09%)	31 / 47 (65.96%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
General disorders and administration			

site conditions			
ENERGY INCREASED			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
FATIGUE			
subjects affected / exposed	4 / 22 (18.18%)	4 / 22 (18.18%)	16 / 47 (34.04%)
occurrences (all)	4	4	17
FEELING HOT			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
PYREXIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	0 / 47 (0.00%)
occurrences (all)	2	1	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			

ANXIETY			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
DEPRESSION			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
EMOTIONAL DISORDER			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3
IRRITABILITY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
MOOD SWINGS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
BLOOD BILIRUBIN UNCONJUGATED INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
HAEMATOCRIT DECREASED			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			

DIZZINESS			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
DYSGEUSIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	5 / 22 (22.73%)	4 / 22 (18.18%)	6 / 47 (12.77%)
occurrences (all)	5	4	6
HYPOAESTHESIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
MIGRAINE			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	2 / 22 (9.09%)	1 / 22 (4.55%)	2 / 47 (4.26%)
occurrences (all)	2	1	3
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			

subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
CONSTIPATION			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	2	0	1
DIARRHOEA			
subjects affected / exposed	1 / 22 (4.55%)	2 / 22 (9.09%)	1 / 47 (2.13%)
occurrences (all)	1	2	1
DYSPEPSIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	4
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
NAUSEA			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	5 / 47 (10.64%)
occurrences (all)	2	2	5
TOOTHACHE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
VOMITING			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
PRURITUS			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	2	0	1
RASH			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Renal and urinary disorders			

POLLAKIURIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
BACK PAIN			
subjects affected / exposed	0 / 22 (0.00%)	4 / 22 (18.18%)	0 / 47 (0.00%)
occurrences (all)	0	4	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
NECK PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			

subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	3 / 47 (6.38%)
occurrences (all)	1	1	4
PHARYNGITIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
SINUSITIS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
TOOTH ABSCESS			
subjects affected / exposed	0 / 22 (0.00%)	0 / 22 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	2 / 47 (4.26%)
occurrences (all)	1	0	2
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	2 / 47 (4.26%)
occurrences (all)	0	1	2

Non-serious adverse events	Arm S1	Arm S2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 145 (53.79%)	32 / 58 (55.17%)	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	2 / 145 (1.38%)	0 / 58 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
ENERGY INCREASED			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
FATIGUE			
subjects affected / exposed	24 / 145 (16.55%)	13 / 58 (22.41%)	
occurrences (all)	25	13	

FEELING HOT			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
PYREXIA			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	3 / 145 (2.07%)	5 / 58 (8.62%)	
occurrences (all)	3	5	
DYSPNOEA			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
NASAL CONGESTION			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 145 (1.38%)	1 / 58 (1.72%)	
occurrences (all)	2	1	
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
RHINORRHOEA			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	6 / 145 (4.14%)	2 / 58 (3.45%)	
occurrences (all)	6	2	
DEPRESSION			
subjects affected / exposed	4 / 145 (2.76%)	1 / 58 (1.72%)	
occurrences (all)	4	1	
EMOTIONAL DISORDER			

subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
INSOMNIA			
subjects affected / exposed	1 / 145 (0.69%)	2 / 58 (3.45%)	
occurrences (all)	1	2	
IRRITABILITY			
subjects affected / exposed	2 / 145 (1.38%)	0 / 58 (0.00%)	
occurrences (all)	2	0	
MOOD SWINGS			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Investigations			
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
BLOOD BILIRUBIN UNCONJUGATED INCREASED			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
HAEMATOCRIT DECREASED			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
WEIGHT DECREASED			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	7 / 145 (4.83%)	2 / 58 (3.45%)	
occurrences (all)	8	2	
DYSGEUSIA			
subjects affected / exposed	3 / 145 (2.07%)	0 / 58 (0.00%)	
occurrences (all)	3	0	
HEADACHE			

subjects affected / exposed	17 / 145 (11.72%)	11 / 58 (18.97%)	
occurrences (all)	19	14	
HYPOAESTHESIA			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
MIGRAINE			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
ABDOMINAL DISTENSION			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
ABDOMINAL PAIN			
subjects affected / exposed	3 / 145 (2.07%)	2 / 58 (3.45%)	
occurrences (all)	3	2	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	1 / 145 (0.69%)	1 / 58 (1.72%)	
occurrences (all)	1	1	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
CONSTIPATION			
subjects affected / exposed	4 / 145 (2.76%)	0 / 58 (0.00%)	
occurrences (all)	4	0	
DIARRHOEA			

subjects affected / exposed	4 / 145 (2.76%)	2 / 58 (3.45%)	
occurrences (all)	4	2	
DYSPEPSIA			
subjects affected / exposed	4 / 145 (2.76%)	2 / 58 (3.45%)	
occurrences (all)	4	2	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	2 / 145 (1.38%)	0 / 58 (0.00%)	
occurrences (all)	2	0	
NAUSEA			
subjects affected / exposed	18 / 145 (12.41%)	5 / 58 (8.62%)	
occurrences (all)	20	7	
TOOTHACHE			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
VOMITING			
subjects affected / exposed	2 / 145 (1.38%)	1 / 58 (1.72%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
PRURITUS			
subjects affected / exposed	3 / 145 (2.07%)	1 / 58 (1.72%)	
occurrences (all)	4	1	
RASH			
subjects affected / exposed	0 / 145 (0.00%)	1 / 58 (1.72%)	
occurrences (all)	0	1	
Renal and urinary disorders			
POLLAKIURIA			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 145 (1.38%)	1 / 58 (1.72%)	
occurrences (all)	2	1	
BACK PAIN			

subjects affected / exposed	6 / 145 (4.14%)	2 / 58 (3.45%)	
occurrences (all)	6	2	
MUSCLE SPASMS			
subjects affected / exposed	2 / 145 (1.38%)	0 / 58 (0.00%)	
occurrences (all)	2	0	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
MYALGIA			
subjects affected / exposed	3 / 145 (2.07%)	2 / 58 (3.45%)	
occurrences (all)	3	2	
NECK PAIN			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
GASTROENTERITIS			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
GASTROENTERITIS VIRAL			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
NASOPHARYNGITIS			
subjects affected / exposed	6 / 145 (4.14%)	1 / 58 (1.72%)	
occurrences (all)	6	1	
PHARYNGITIS			
subjects affected / exposed	0 / 145 (0.00%)	0 / 58 (0.00%)	
occurrences (all)	0	0	
SINUSITIS			

subjects affected / exposed	3 / 145 (2.07%)	0 / 58 (0.00%)	
occurrences (all)	3	0	
TOOTH ABSCESS			
subjects affected / exposed	1 / 145 (0.69%)	0 / 58 (0.00%)	
occurrences (all)	1	0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	10 / 145 (6.90%)	3 / 58 (5.17%)	
occurrences (all)	10	3	
URINARY TRACT INFECTION			
subjects affected / exposed	7 / 145 (4.83%)	0 / 58 (0.00%)	
occurrences (all)	7	0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	3 / 145 (2.07%)	3 / 58 (5.17%)	
occurrences (all)	3	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 August 2014	The purpose of this amendment was as follows: - Added Arm G to evaluate ABT-493 (200 mg) once daily (QD) and ABT-530 (40 mg) QD in treatment-naïve and pegylated interferon/ribavirin experienced HCV GT3-infected subjects. - Extended Screening Period duration limit from 35 to 42 days to minimize the risk of screen failing subjects due to screening window duration.
11 November 2014	The purpose of this amendment was as follows: - Removed 60% enrollment cap on treatment-naïve (TN) subjects. - Clarified the assessment of adverse events (AE) relatedness to the AbbVie direct-acting antiviral agent (DAAs) and ribavirin (RBV). - Updated the resistance analyses to include phylogenetic analysis of viral subtypes so that treatment efficacy (sustained virologic response 12 weeks postdosing, SVR12) could be compared across the different subtypes in the study.
20 February 2015	The purpose of this amendment was as follows: - Added new genotype (GT) 2 arm (Arm J) to evaluate ABT-493 (300 mg) + ABT-530 (120 mg) to understand if a higher dose of ABT-493 in combination with ABT-530 (120 mg) would result in improved sustained virologic response (SVR) while maintaining safety and tolerability. - Changed doses to be evaluated in GT3 Arms L, O, and P (Part 2) from ABT-493 (200 mg) + ABT-530 (40 mg) to ABT-493 (300 mg) + ABT-530 (120 mg) to understand if a higher dose of ABT-493 in combination with ABT-530 (120 mg) would result in improved SVR for 8-week treatment durations in subjects without cirrhosis or in a harder-to-treat population (subjects with cirrhosis) with a 12-week treatment duration. - Added a potential method (deep sequencing) to sequence hepatitis C virus (HCV) samples.
26 February 2015	The purpose of this amendment was as follows: - Clarified efficacy enablement criteria to enable enrollment of Arm I for GT2-infected subjects and Arms K, M, and N for GT3-infected subjects. - Clarified that safety enablement criteria were dependent on the number of subjects with AEs (with reasonable possibility of being related to the DAAs) leading to study drug discontinuation.
10 April 2015	The purpose of this amendment was as follows: - Modified ABT-530 dose for Arms M and N to be evaluated in combination with 200 mg ABT-493 in GT3-infected cirrhotic cohorts to understand if an 80 mg dose of ABT-530 would maintain high SVR rates while maximizing the safety and tolerability of the regimen. - Provided additional data for the ABT-493 exposure- alanine aminotransferase (ALT) level and ABT-493 exposure-total bilirubin level relationships with respect to Grade 2 ALT and total bilirubin elevations, respectively. - Updated aminotransferase/platelet ratio index (APRI) cutoff value in Inclusion Criterion for defining noncirrhotic in Part 2 to reflect a more accurate APRI cutoff value. - Updated text in Exclusion Criterion and added justification to allow enrollment of subjects on stable opioid replacement therapy of methadone or buprenorphine ± naloxone for at least 6 months prior to screening following availability of preliminary pharmacokinetic, pharmacodynamic, and safety data from Study M13-602. - Provided clarification on the requirements for additional liver diagnostic testing in subjects in Part 2 with a previous diagnosis of cirrhosis by biopsy. - Clarified toxicity management and additional clinical guidance with respect to ribavirin (RBV) dose modification.

03 September 2015	The purpose of this amendment was as follows: - Updated preliminary results for Part 1 and enrollment status of Part 2. - Updated the sample size for Arm J in Part 2 to accurately reflect the enrollment numbers. - Increased the sample size for Arm L in Part 2 and extend treatment duration for pegylated interferon/ribavirin (PR)-experienced subjects in Arm L to 12 weeks. - Restricted enrollment of Arms M – P (12 week treatment duration) in Part 2 to treatment-naïve (TN) cirrhotic subjects and extended the treatment duration for treatment-experienced (TE) cirrhotic subjects previously enrolled in Arm O under Protocol Amendment 5 to 16 weeks to determine the optimal dosing regimen in cirrhotic subjects who were TN. - Updated inclusion criteria for TE subjects in Part 2. - Updated AE collection period to reflect the continued collection of serious adverse events (SAEs) from 30 days after drug stopped through the end of the study.
30 September 2015	The purpose of this amendment was as follows: - Updated with preliminary results for Part 2 of the study. - Added study design for Part 3 and prespecified criteria to enable Part 3 evaluation. - Expanded the eligibility criteria for enrollment of subjects in Part 3 to facilitate evaluation of subjects' representative of the targeted HCV-infected population and to broaden the definition of treatment experience to include those who previously received sofosbuvir plus ribavirin with or without pegylated interferon therapy. - Updated text describing the use of coformulated ABT-493/ABT-530 tablets in Part 3 (dosing and the requirement to take the tablets with food). - Updated the management of increases in alanine aminotransferase (ALT) for Part 3 to reflect inclusion of HCV-infected patients with ALT levels up to < 10 upper limit of normal (ULN). - Provided clarification regarding management of prohibited therapy and concomitant medications. - Updated Inclusion Criteria and urine pregnancy test requirements for Part 3 of the study to provide time requirements for effective methods of contraception during the study and frequency of urine pregnancy tests in the Post-Treatment Period for subjects in Part 3 who were no longer being administered RBV. Provided a list of the effective methods of birth control for subjects and their partners. - Updated Inclusion Criterion with regards to FibroScan requirements in Part 3 to allow any historical FibroScan for subjects with an existing diagnosis of cirrhosis prior to screening. - Clarified the treatment extension criteria for subjects in Part 2 and provided the treatment extension criteria for subjects in Part 3.
16 December 2015	The purpose of this amendment was as follows: - Updated with preliminary results for Part 2 of the study and clarified that Arms M and N in Part 2 would not be opened. - Specified which arms and GT3-infected subpopulations would be evaluated in Part 3, based on the supporting data from Part 2. - Added study design for Part 4 based on data from Study M14-867 and Arm J in Part 2. - Updated Inclusion Criteria, and Exclusion Criteria to clarify that subjects without cirrhosis enrolled in Part 3 had to be TE, to clarify the methods for assessment of liver fibrosis in the setting of an indeterminate Fibrotest score, and to clarify which cohorts and parts the laboratory eligibility criteria were applicable to. - Clarified treatment extension criteria for subjects in Part 3 and provided the treatment extension criteria for subjects in Part 4. - Updated guidance for the investigator in the setting of a subject pregnancy in Parts 3 and 4, in which RBV was not administered. Clarified the time period during the study for which female subjects and male subjects (and their female partners) were to avoid pregnancy. - Clarified that Sanger sequencing would be performed in the setting of a result of "unable to genotype" but not for "unable to subtype."

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27456384